

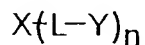
RESPONSE TO RESTRICTION REQUIREMENT  
U.S. Appln. No. 10/536,504 (Q88025)

AMENDMENTS TO THE CLAIMS

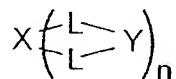
This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

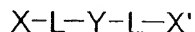
Claim 1. (Original) A prodrug of the general Formula (I), (II) or (III):



(I)



(II)



(III)

in which

X is a tobramycin moiety;

X' is a pharmaceutically active moiety;

L is a linker group;

Y is a pharmacokinetic regulator; and

n is an integer of 1 or greater

or a pharmaceutically acceptable derivative or salt thereof.

Claim 2. (Previously Presented) A prodrug according to claim 1, wherein the pharmaceutically active moiety is selected from the group consisting of an aminoglycoside, nucleoside, rhinovirus capsid-binding compound, antisense oligonucleotide,

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peptide, an inhibitor of HIVRT, an inhibitor of influenza neuraminidase, amphotericin  $\beta$ , an azole and an aspartic proteinase.

Claim 3. (Previously Presented) A prodrug according to claim 2, wherein the aminoglycoside is selected from the group consisting of tobramycin, kanamycin A to C, amikacin, neomycin, streptomycin, neamine, paromomycin, lividomycin, 2230-C, ribostamycin, xyllostasin, butirosin, 4'-deoxybutyrosin, LL-BM408a, gentamycins and nebramycin.

Claim 4. (Previously Presented) A prodrug according to claim 3, wherein the aminoglycoside is selected from the group consisting of tobramycin, amikacin, neomycin and kanamycin.

Claim 5. (Previously Presented) A prodrug according to claim 3 or claim 4, wherein the aminoglycoside is tobramycin.

Claim 6. (Previously Presented) A prodrug according to claim 1, wherein the linker group is selected from the group consisting of esters, amides, ureas, thioureas, imines, acetals, ethers, phosphates, phosphate esters or diesters, thioesters, oximes and hydrazones.

Claim 7. (Previously Presented) A prodrug according to claim 6, wherein the linker group is selected from the group consisting of an ester, amide, oxime and phosphate.

Claim 8. (Previously Presented) A prodrug according to claim 2, wherein the linker group is an ester.

Claim 9. (Previously Presented) A prodrug according to claim 1, wherein the pharmacokinetic regulator Y is a hydrophobic or hydrophilic moiety.

Claim 10. (Previously Presented) A prodrug according to claim 9, wherein the hydrophobic moiety is an optionally

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substituted straight chain, branched and/or cyclic saturated or unsaturated hydrocarbon.

Claim 11. (Previously Presented) A prodrug according to claim 10, wherein the hydrophobic moiety is an optionally substituted alkyl or optionally substituted alkenyl having 1 to 24 carbon atoms which is optionally interrupted with oxygen or nitrogen; an optionally substituted aryl; or an optionally substituted heterocyclyl.

Claim 12. (Previously Presented) A prodrug according to claim 11, wherein the optionally substituted alkyl or the optionally substituted alkenyl is an optionally substituted C<sub>1-20</sub> alkyl or optionally substituted C<sub>2-20</sub> alkenyl which is optionally interrupted with O, C=O, NH, optionally substituted aryl or optionally substituted heterocyclyl and optionally substituted with carboxyl, optionally substituted C<sub>1-6</sub> alkyl, amino or hydroxyl.

Claim 13. (Previously Presented) A prodrug according to claim 11, wherein the optionally substituted aryl is an optionally substituted phenyl or optionally substituted biphenyl.

Claim 14. (Previously Presented) A prodrug according to claim 11, wherein the optionally substituted heterocyclyl is a 5- or 6-membered nitrogen containing heterocyclic group.

Claim 15. (Previously Presented) A prodrug according to claim 14, wherein the heterocyclic group is selected from the group consisting of pyridyl, indolyl, indazolyl, 2,3-dihydro-1H-indolyl, furanyl, isoxazolyl, pyrazolyl and thiofuranyl.

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Claim 16. (Currently Amended) A prodrug according to claim 13, wherein the optional substituents on the phenyl or heterocyclyl are selected from the group consisting of halo, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkoxy, hydroxy and OCF<sub>3</sub>.

Claim 17. (Previously Presented) A prodrug according to claim 9, wherein the hydrophilic moiety is selected from the group consisting of oligonucleotides up to 20 nucleotides in length, peptides up to 20 amino acids in length, peptide mimics, carbohydrates, oligosaccharides and derivatives thereof.

Claim 18. (Previously Presented) A method for the preparation of the prodrug of Claim 1 comprising the steps of:

(a) optionally protecting the moieties X and/or X' and/or the linker group which is attached to the optionally protected pharmacokinetic regulator Y;

(b) reacting the optionally protected moieties X and/or X' and the optionally protected linker group L attached to the optionally protected pharmacokinetic regulator Y; and

(c) if necessary, removing the protecting groups of the moieties X and/or X', the linker L and the pharmacokinetic regulator Y.

Claim 19. (Previously Presented) A pharmaceutical formulation comprising the prodrug of claim 1 or a pharmaceutically acceptable salt or derivative thereof, together with one or more pharmaceutically acceptable carriers.

Claim 20. (Previously Presented) A pharmaceutical formulation according to claim 19, which further comprises one or more other therapeutic and/or prophylactic ingredients.

Claim 21. (Previously Presented) A pharmaceutical formulation according to claim 20, wherein the other therapeutic

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and/or prophylactic ingredients is an antimicrobial or antiinfective agent.

Claim 22. (Previously Presented) A pharmaceutical formulation according to claim 21, wherein the antiinfective agent is an antibacterial agent.

Claim 23. (Previously Presented) A pharmaceutical formulation according to claim 22, wherein the antibacterial agent is effective to treat respiratory infections.

Claim 24. (Previously Presented) A pharmaceutical formulation according to claim 22, wherein the antibacterial agent is a combination selected from the group consisting of trimethoprim and sulfonamide; bacitracin and polymyxin B-neomycin; imipenem and fluoroquinolone; and beta-lactam and aminoglycosides.

Claim 25. (Previously Presented) An inhaler which comprises a prodrug of claim 1.

Claim 26. (Previously Presented) An inhaler according to claim 25, wherein said inhaler is adapted for oral administration as a free-flow powder.

Claim 27. (Previously Presented) An inhaler according to claim 25, wherein said inhaler is a metered dose aerosol inhaler.

Claim 28. (Previously Presented) A method for the prevention and/or treatment of a microbial infection comprising the step of administration to a subject in need thereof of an effective amount of the prodrug of claim 1.

Claim 29. (Previously Presented) A method according to claim 28, wherein the microbial infection is a bacterial infection.

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Claim 30. (Previously Presented) A method according to claim 29, wherein the infection is a Gram Negative or Gram Positive infection.

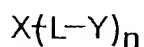
Claim 31. (Previously Presented) A method according to claim 30, wherein the bacterial infection is associated with the respiratory tract, urinary tract or GI tract or a systemic infection caused by enteric bacteria.

Claim 32. (Previously Presented) A method according to claim 28, wherein the administration is to the respiratory tract by inhalation, insufflation or intranasally or a combination thereof.

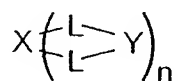
Claims 33-36. (Cancelled).

Claim 37. (Previously Presented) A method for the detection of a microbial infection which comprises the step of contacting the prodrug of claim 1 with a sample suspected of containing the microorganism.

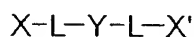
Claim 38. (Original) A prodrug of general Formula (I), (II) or (III):



(I)



(II)



(III)

in which

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X and X' are either the same or different and selected from an aminoglycoside excluding tobramycin;

L is a linker group excluding amide and carbamate;

Y is a pharmacokinetic regulator; and

n is an integer of 1 or greater

or a pharmaceutically acceptable derivative or salt thereof.

Claim 39. (Previously Presented) A prodrug according to claim 38, wherein the aminoglycoside X is selected from the group consisting of kanamycin A to C, amikacin, neomycin, streptomycin, neamine, paromomycin, lividomycin, 2230-C, ribostamycin, xyllostasin, butirosin, 4'-deoxybutyrosin, LL-BM408a, gentamycins and nebramycin.

Claim 40. (Previously Presented) A prodrug according to claim 39, wherein the aminoglycoside is selected from the group consisting of amikacin, neomycin and kanamycin.

Claim 41. (Previously Presented) A prodrug according to claim 38, wherein the linker group is selected from the group consisting of esters, ureas, thioureas, imines, acetals, ethers, phosphates, phosphate esters or diesters, thioesters, oximes and hydrazones.

Claim 42. (Previously Presented) A prodrug according to claim 41, wherein the linker group is selected from the group consisting of an ester, oxime and phosphate.

Claim 43. (Previously Presented) A prodrug according to claim 41, wherein the linker group is an ester.

Claim 44. (Previously Presented) A prodrug according to claim 38, wherein the pharmacokinetic regulator is a hydrophobic or hydrophilic moiety.

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Claim 45. (Previously Presented) A prodrug according to claim 44, wherein the hydrophobic moiety is an optionally substituted straight chain, branched and/or cyclic saturated or unsaturated hydrocarbon.

Claim 46. (Previously Presented) A prodrug according to claim 45, wherein the hydrophobic moiety is an optionally substituted alkyl optionally substituted alkenyl having 1 to 24 carbon atoms which is optionally interrupted with oxygen or nitrogen; an optionally substituted aryl; or an optionally substituted heterocyclyl.

Claim 47. (Previously Presented) A prodrug according to claim 46, wherein the optionally substituted alkyl or optionally substituted alkenyl is an optionally substituted C<sub>1-20</sub> alkyl or optionally substituted C<sub>2-20</sub> alkenyl which is optionally interrupted with O, C=O, NH, optionally substituted aryl or optionally substituted heterocyclyl and optionally substituted with carboxyl, optionally substituted C<sub>1-6</sub> alkyl, amino or hydroxyl.

Claim 48. (Previously Presented) A prodrug according to claim 46, wherein the optionally substituted aryl is an optionally substituted phenyl or optionally substituted biphenyl.

Claim 49. (Previously Presented) A prodrug according to claim 46, wherein the optionally substituted heterocyclyl is a 5- or 6-membered nitrogen containing heterocyclic group.

Claim 50. (Previously Presented) A prodrug according to claim 49, wherein the heterocyclic group is selected from the group consisting of pyridyl, indolyl, indazolyl,

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2,3-dihydro-1H-indolyl, furanyl, isoxazolyl, pyrazolyl and thiofuranyl.

Claim 51. (Previously Presented) A prodrug according to claim 48, wherein the optional substituents on the phenyl or heterocyclyl are selected from the group consisting of halo, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkoxy, hydroxy and OCF<sub>3</sub>.

Claim 52. (Previously Presented) A prodrug according to claim 44, wherein the hydrophilic moiety is selected from the group consisting of oligonucleotides up to 20 nucleotides in length, peptides up to 20 amino acids in length, peptide mimics carbohydrates, oligosaccharides and derivatives thereof.

Claim 53. (Previously Presented) A method for the preparation of the prodrug of claim 38 comprising the steps of:

(a) optionally protecting the moieties X and/or X' and/or the linker group which is attached to the optionally protected pharmacokinetic regulator Y;

(b) reacting the optionally protected moieties X and/or X' and the optionally protected linker group L attached to the optionally protected pharmacokinetic regulator Y; and

(c) if necessary, removing the protecting groups of the moieties X and/or X' the linker L and the pharmacokinetic regulator Y.

Claim 54. (Previously Presented) A pharmaceutical formulation comprising the prodrug of claim 38 or a pharmaceutically acceptable salt or derivative thereof, together with one or more pharmaceutically acceptable carriers.

Claim 55. (Original) A pharmaceutical formulation according to claim 54, which further comprises one or more other therapeutic and/or prophylactic ingredients.

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Claim 56. (Previously Presented) A pharmaceutical formulation according to claim 55, wherein the other therapeutic and/or prophylactic ingredients is an antimicrobial or antiinfective agent.

Claim 57. (Previously Presented) A pharmaceutical formulation according to claim 56, wherein the antiinfective agent is an antibacterial agent.

Claim 58. (Previously Presented) A pharmaceutical formulation according to claim 57, wherein the antibacterial agent is effective to treat respiratory infections.

Claim 59. (Previously Presented) A pharmaceutical formulation according to claim 57, wherein the antibacterial agent is a combination selected from the group consisting of trimethoprim and sulfonamide; bacitracin and polymyxin B-neomycin; imipenem and fluoroquinolone; and beta-lactam and aminoglycosides.

Claim 60. (Previously Presented) An inhaler which comprises a prodrug of claim 38.

Claim 61. (Previously Presented) An inhaler according to claim 60, wherein said inhaler is adapted for oral administration as a free-flow powder.

Claim 62. (Previously Presented) An inhaler according to claim 60, wherein said inhaler is a metered dose aerosol inhaler.

Claim 63. (Previously Presented) A method for the prevention and/or treatment of a microbial infection comprising the step of administration to a subject in need thereof of an effective amount of the prodrug of claim 38.

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Claim 64. (Previously Presented) A method according to claim 63, wherein the microbial infection is a bacterial infection.

Claim 65. (Previously Presented) A method according to claim 64, wherein the bacterial infection is a Gram Negative or Gram Positive infection.

Claim 66. (Previously Presented) A method according to claim 65, wherein the bacterial infection is associated with the respiratory tract, urinary tract or GI tract or a systemic infection caused by enteric bacteria.

Claim 67. (Previously Presented) A method according to claim 63 wherein the administration is to the respiratory tract by inhalation, insufflation or intranasally or a combination thereof.

Claims 68-71. (Cancelled).

Claim 72. (Previously Presented) A method for the detection of a microbial infection which comprises the step of contacting the prodrug of claim 38 with a sample suspected of containing the microorganism.

Claims 73-105. (Cancelled).